REMARKS AND ARGUMENTS

Claims 1-2, 6-7, 12-13, 25, 27, and 29-42 are under examination. Claims 3-5, 8-11, and 14-24 have been withdrawn as not reading on the elected species. Claims 1, 25, and 27 have been amended for improved clarity. Claims 26 and 28 have been canceled without prejudice. No new matter has been added with this Amendment.

Election/Restrictions:

Applicants acknowledge that a new species was elected and examined along with the initially elected species. Thus, the species under examination are those in which X is CHCHBr or CHCHI, Y is H, R' is $CH_2(CH2)_4F$ or the N2S2 chelate shown and R" is CH_3. Accordingly, claims 1-2, 6-7, 12-13, 25, 27, and 29-42 are under examination.

Claim Rejections under 35 U.S.C. § 102:

Claims 25-28 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Kuhar (United States Patent No. 5,413,779). Applicants respectfully traverse this rejection.

The Office Action alleges that Kuhar discloses a compound having the structure shown in column 3, line 50, which is within the scope of the formula in claims 25-28.

Without acquiescing to this rejection and in the interest of advancing prosecution of this application, claims 25 and 27 have been amended to better claim the subject matter which Applicants regard as the invention. Claims 26 and 28 have been canceled without prejudice. The amended claims are directed to the kits containing components useful for synthesizing various radioactive 4-haloethenylphenyl tropanes. These tropane compounds bind to serotonin transporters specifically and selectively as illustrated in the Specification (*see* Tables 1 and 8). Therefore, these tropane compounds when labeled with a radioactive halogen are useful in imaging methods such as PET and SPECT. Amended claim 25 specifically defines that a

leaving group, L, is displaced with a substituent containing a radioactive group such as -CH_2CH_2Q, -CHCHR or -CCH_2FCH_2 where Q is ^{18}F or $CH_2{}^{18}F$, R is ^{123}I, ^{125}I, ^{131}I, ^{75}Br, ^{76}Br, ^{77}Br, ^{82}Br, ^{18}F or $CH_2{}^{18}F$. Similarly, amended claim 27 specifies that a leaving group, L, is displaced with a substituent of $CH_2(CH_2)n^{18}F$.

Claims 25 and 27 as amended are not anticipated by Kuhar. Kuhar describes a compound, 3 -[4-iodophenyl]-tropan-2 -carboxylic acid methyl ester (RTI 55) as a high affinity binding ligand for dopamine and serotonin transporters. 3 -(trimethyltinphenyl)-tropan-2 -carboxylic acid ester, the compound alleged to be within the scope of the formula of claims 25-28 (amended claims 25 and 27), is an intermediate for synthesizing [^{123}I]-RTI 55 or [^{125}I]-RTI 55. The compounds synthesized using the claimed kits are different from those described by Kuhar, structurally and biologically. The compounds synthesized by the claimed kits contain haloalkyl or haloalkenyl substitution at the 4-position and optionally halogen substitution at the 3-position in the benzyl ring. By contrast, the alleged compound in Kuhar is an intermediate for synthesizing a compound with halogen substitution, **not** alkylhalogen or alkenylhalogen, at the 4-position in the benzyl ring (*see* the diagram in columns 5 and 6). This difference is reflected in the components of the kits in amended claims 25 and 27. Because of this difference, Kuhar does not teach all of the components of the claimed kits. Moreover, there is no teaching in Kuhar that the alleged compound can be used to synthesize the claimed tropane compounds with haloalkyl or haloalkenyl substitution in the phenyl ring. The specific biological activities of these compounds are accounted for by the structural characteristics of these compounds; the Kuhar compounds bind to both serotonin and dopamine transporters whereas the claimed compounds of the instant application bind selectively and specifically to serotonin transporters. The inventors herein demonstrated this selective activity of the compounds disclosed herein for the first time.

Based on the foregoing, applicants submit that a person of ordinary skill in the art would not have been able to make and use the claimed kits based on the teachings of Kuhar. Accordingly, claims 25 and 27 as amended are not anticipated by Kuhar.

The Office Action further alleges, based on the decision in *re Hutchison,* 69 USPQ 138, that the usage of the phrase, "capable of" in the claims is not a positive limitation and does not constitute a limitation in any patentable sense. Applicants submit the following response for the allegation.

In the cited case, the functional term, "adapted for use" was used to indicate that the claimed article is "adapted" for specific use. Thus, the term used indeed did not constitute a limitation in any patentable sense.

In contrast, the term, "capable of", as recited in amended claims 25 and 27, was used to indicate that the reagent included in the claimed kit is able to displace the leaving group with the substituent containing a radiotracer atom. The usage of "capable of" describes the very function/property of the reagent, i.e., it is clear to one of ordinary skill in the art that a reagent is chosen because of its capability of displacing one group with the other to make the desired compound. This is consistent with the decision in *re. Swinehart et al.* 169 USPQ 226 (CCPA 1971) which held that functional terms, such as "adapted for", "effective amount", "detent mechanism" and the like are not *per se* objectionable in claims unless the language used is not precise and definite enough to provide a clear-cut indication of the scope of the subject matter embraced by the claim. Applicants submit that the recitation of "capable of" in claims 25 and 27 is consistent with the above criteria.

Based on the foregoing, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b).

Claim Rejections under 35 U.S.C. § 103:

Claims 1-2, 6-7, 12-13, and 25-38 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Kung (United States Patent No. 6,241,963) in view of Davies (United States Patent No. 6,013,242). Applicants respectfully traverse this rejection.

The Office Action alleges that Kung discloses tropane derivative compounds of formula 1 in column 5, which are similar to the claimed compounds. The Office Action further asserts that Davies discloses tropane derivative compounds analogous to those taught by Kung and the advantage of modifying tropane compounds and thus it would have been obvious to one of ordinary skill in the art to modify the compounds disclosed by Kung to include a moiety encompassed by "X" as claimed, such as CHCHI, based on the teachings of Davies.

Applicants disagree with the above allegation. The compounds claimed in the present application are distinct from the compounds disclosed in Kung. The invention claimed is directed to a series of compounds in the 4-haloethenylphenyl tropane family (e.g., -CHCHI or CHCHBr substituted in the para position of the phenyl ring), which bind to serotonin transporters with high selectivity and specificity. In contrast, the tropane compounds disclosed in Kung contain the phenyl ring substituted with hydrogen, alkyl or halogen. It is stated therein that "... that the novel ligands of the invention are selective for CNS receptors, particularly dopamine receptors..." (*see* column 7, lines 31-33, underline added for emphasis). Therefore, the compounds claimed herein are structurally and functionally different from those taught by Kung. There is no suggestion in the Kung patent that the tropane compounds disclosed therein can be substituted in the para position of the phenyl ring with a haloethenyl group to exhibit selective binding to serotonin transporters with high affinity as taught in the present application.

The compounds disclosed in Davies are distinct from those claimed in the present invention; the tropane derivatives of Davies contain with $-COR_5$ substitution in the 2-beta position wherein R_5 is H or alkyl (C1-8). By contrast, the claimed compounds in the present application contain carbomethoxy group (i.e., $COOCH_3$) in the 2-beta position of the tropane backbone. There is nothing in Davies which suggests that the 2-beta position of the compounds disclosed therein can be substituted with an ester group to exhibit selective binding to serotonin transporters as taught in the present application. The Davies patent does not provide motivation to a person of ordinary skill in the art to combine the teachings therein with those of Kung to make the claimed invention.

A rejection for obviousness over a combination of references cannot be sustained unless some motivation to combine the teachings therein can be found within the references themselves. *See* In *re Lee*, 61 USPQ 2d 1430 (Fed. Cir. 2002). Kung describes certain tropane compounds with alkyl- or halo-phenyl ring, which are ligands for CNS receptors, particularly dopamine receptors. Davies discloses certain tropane compounds with -COR substitution in the 2-beta position that bind the 5-HT or dopamine reuptake site differentially. Neither of the cited patents teaches nor suggests the compounds claimed in the present application. Neither Kung nor Davies suggests any modifications or a need to modify their compounds to make the claimed compounds of 4-haloethenylphenyl tropanes. There is nothing in Kung or Davies that would motivate one skilled in the art to combine the teachings of the cited references to make the claimed invention. The inventors herein are the first to demonstrate that the ester group in the claimed compounds is crucial in both providing high binding affinity and selectivity to the serotonin transporters as well as high brain penetrance and specific binding in serotonin transporter-rich brain tissues. In addition, the combination of the haloethenyl group and the ester group provide excellent physiochemical properties that were not taught or suggested in the Kung or Davies patent.

Based on the foregoing, Applicants respectfully submit that the invention is not *prima facie* obvious over Kung in view of Davies. Withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Claim Objections:

Claims 25-28 are objected to under 37 C.F.R. 1.75 as allegedly being of improper dependent form.

Claims 25 and 27 have been amended and rewritten as independent claims to address the issues raised in the Office Action. Claims 26 and 28 have been canceled without prejudice. Therefore, this objection is no longer applicable. Withdrawal of the claim objection is respectfully requested.

Allowable Subject Matter:

Claims 39-42 have been viewed as allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

In view of the amendments made in the present Response, Applicants respectfully request reconsideration of the claims as amended along with claims 39-42, and allowance of all the claims under examination.

Conclusion:

Based on the foregoing amendments and arguments, this case is considered to be in condition for allowance and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone call is requested, and the Examiner is invited to call to arrange a mutually convenient time.

It is believed that no fee is due with this submission; however, if this is incorrect, please deduct the appropriate fee for this submission and any extension of time required from Deposit Account No. 07-1969.

Respectfully submitted,

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